COMPARATIVE STUDY OF THROMBOLYTIC THERAPY AND NON THROMBOLYTIC THERAPY IN THE MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

THESIS

FOR

DOCTOR OF MEDICINE

(INTERNAL MEDICINE)

BUNDELKHAND UNIVERSITY
JHANSI (U. P.)

1996 **VIMAL KUMAR**

Dedicated this thesis to the

people who died in the

disastrous of

Hiroshima

&

Nagasaki

CERTIFICATE

This is to certify that the work entitled"COMPARATIVE STUDY OF THROMBOLYTIC THERAPY AND NON THROMBOLYTIC THERAPY IN THE MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION" which is being submitted as a thesis for M.D. (Medicine) Examination, 1996 of Bundelkhand University, Jhansi has been carried out by Dr. VIMAL KUMAR has been carried out in the Department of Medicine, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the department as per university regulations.

Dated : 28.11.95

(R. C. Arora)
M.D., D. Sc.,
Professor and Head,
Department of Medicine,
M. L. B. Medical College,
Jhansi.

CERTIFICATE

This is to certify that the work entitled"COMPARATIVE STUDY OF THROMBOLYTIC THERAPY AND NON THROMBOLYTIC THERAPY IN THE MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION" which is being submitted as a thesis for M.D. (Medicine) Examination of Bundelkhand University, has been carried out by Dr. VIMAL KUMAR under my direct supervision and guidance. The techniques embodied in the thesis were undertaken by the candidate himself and observations recorded have been checked by me from time to time.

Dated: 28.11.95

(Praveen Kumar)
M.D., D. M. (Card.),
Assistant Professor,
Cardiology,
Department of Medicine,
M.L.B. Medical college,
(GUIDE)

ACKNOWLEDGEMENT

It is with a heart filled with profound gratitude that I endeavour to thank all, who have extended their help towards my academic venture.

I wish to express my heartfelt thankfulness to my Guide Dr. Praveen Kumar, MD, DM (Card.), Assistant Professor and Incharge Cardiology Unit, Department of Medicine, M.L.B. Medical College, Jhansi for his keen interest and helpful suggestions, thus making my venture a successful one.

I wish to express my humble gratitude to my esteemed learned teacher Dr. R. C. Arora, M.D., D. Sc., professor and Head, Department of Medicine, M.L.B. Medical College, Jhansi, Not only for his invaluable guidance but also for his constant encouragement and constructive criticism. I am indebted to him for sharing with me his treasure of knowledge and expereince.

I would also like to thank Dr. D. N. Mishra, MD, MNAMS, Professor, Dr. P. K. Jain, MD, MNAMS, Associate Professor, Dr. N. Agarwal (MD) Asst. Professor, Dr. G. D. Shukla MD, MNAMS, Department of Medicine, M.L.B. Medical College, Jhansi for their encouraging and helpful attitude.

My fellow residents specially Dr. R.S. Madhoria Dr. Narendra Deo and Dr. Anil Nirwan, Dr. Amitabh Upadhyay have helped me in many ways to accomplish this project. My sincere thanks to them.

I wholeheartedly thank to Mr. Alok Kumar Gupta for his hardwork in processing and comilation of my thesis.

Last but not the least I wish to thank my parents, who always stood by me, showering on me their abundant affection and blessings thereby shaping me into a worthy human being.

Dated : 28.11.95

(VIMAL KUMAR)

CONTENTS

CHAPTER	PAGE NO.
INTRODUCTION	1 - 12
REVIEW OF LITERATURE	13 - 21
AIMS OF STUDY	22 - 22
MATERIAL & METHODS	23 - 25
OBSERVATION	26 - 38
DISCUSSION	39 - 46
SUMMARY & CONCLUSION	47 - 49
REFERENCES	ONWARDS

INTRODUCTION

INTRODUCTION

Ischaemic heart disease is first leading cause of death in western countries. In United States Approximately 1.5 million myocardial infarction cases occur each year. The mortality with acute myocardial infarction is approximately 30 percent with more than half of the deaths occurring before the striken individual reaches the hospital. Several studies have shown that survival following hospitalization has improved over the last two decades. An additional 5-10 percent of survivors die in the first year following myocardial infarction.

Myocardial infarctin generally results from abrupt decrease in coronary blood flow. This generally follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis. The progression of atherosclerotic lesion to the point where thrombus formation occurs is a complex process related to vascular injury. The injury is produced or facilitated by factors such as cigarette smoking, hypertension and lipid accumulation in the majority of cases. Infarction occurs when an atherosclerotic plaque fissures, reptures or ulcerates and with conditions favouring thrombogenesis (Factors which may be local or systemic). A mural thrombus forms leading to coronary artery occlusion. In rare cases infarction may be due to coronary artery occlusion secondary to coronary

emboli, congenital abnormalities, coronary spasm and wide variety of systemic diseases particularly of inflammatory naturae. Ultimately the amount of myocardial damage caused by the affected vessels, whether or not the vessel becomes totally occluded. Patients at increased risk of developing acute myocardial infarction include those with unstable angina, multiply coronary risk factors and prinzmetal's variant angina. Less common etiological factors includes hypercoagulability, coronary embolicollagen vascular disease and cocain abuse. The acute myocardial infarction can be precipitated by some factors these are physical exercise, emotional stress and medical or surgical illnesses. The onset of myocardial infarction may be at any time being more commonn and earliest symptoms of acute myocardial infarction. The intensity of pain varies with great deal, and although it is severe excruciating and heavy squeezing type. The pain of acute myocardial infarction is more severy and persist longer than the pain of angina pectoris. Pain occurs at centre of chest/epigastrium and is 30 percent cases radiates to the arm, less common sites of radiation of pain include, abdomen, back, lower jaw and neck. The pain is followed by weakness, sweating, nausea, vomiting, giddiness, and anxiety and discomfort at rest. But about 15-20 percent of myocardial infarctions are painless. The incidence of painless infarction is greater in diabetes mellitus and it increases with age . In elderly patients acute myocardial infarction may present as sudden onset of breathlessness which may progress to

pulmonary oedema. Other less common presentations of acute myocardial infarction are sudden loss of consciousness and confusional state. The pain of acute myocardial infarction is similar to the pain of acute pericarditis, pulmonary embolism, acute aortic dissection or costochondritis. In physical findings, the patient is anxious, restless and attempting to relieve the pain by moving about in bed, squirming and stretching. Pallor is common and is often associated with perspiration of substernal chest pain persisting more than 30 minutes and diaphoresis strongly suggests acute myocardial infarction. About 1/4 th patients of anterior infarction have tachycadia and hypertension and upto 1/2 with inferior infarction shows evidence of bradycardia and hypotension. The apex beat is difficult to palpate. Third heart shound (S_3) and fourth heart sound (S_4) are present and the first heart sound (S_1) and second heart sound (S_2) are diminished in intensity. Rarely paradoxical splitting of second heart sound. A transient apical systolic murmur due to mitral regurgitation and dysfunction of papillary muscle is commonly seen during acute infarction. Pericardial friction rub is found in many patients of transmural myocardial infarction. Jugular venous distension occurs commonly in patients with right ventricular infarction, carotid pulse is often decreased in volume, reflecting reduced stroke volve. Temperature upto 38 ^{o}C elevated during the first week of acute myocardial infarction. The acute myocardial infarction is diagnosed by :

1. Non specific indices of tissue necrosis and inflammation - A non - specific reaction to myocardial injury is associated with polymorphonuclear leukocytosis and it often reaches levels of 12000 - 15000

   — leukocytes per ml, the ESR rises more slowly than W. B. C.

2. The electrocardiographic manifestation of acute myocardial infarction - Transmural infarction is often present if ECG shows Q wave or loss of R wave and non transmural infarction may be present if ECG, shows only ST segment and / or T wave changes which persist.

3. Serum enzymes changes - Enzymes are released in large quantities into the blood from necrotic heart muscles following myocardial infarction.

   A. Estimation of SGOT and SGPT : The isoenzyme of CK / LDH has the advantage over CK and LDH in that these are not present in significant concentration in extracardias tissues and therefore are more specific.

   B. Creatine phosphokinase (CPK) rises withing 8-24 hours and generally returns to normal by 48-72 hours except in large infarction.

   C. Lactic dehydrogenase (LDH) rises later (24-48 hours) and remains elevated for as long as 7 to 14 days.

The myocardial specificity of the insoenzyme determined by the use of radioimmunoassay technique or gel electrophoresis technique for LDH. The isoenzyme which predominates in the heart is referred to as LDH_1 other potential sources of total CK elevation are :

a. Musclar disease includes muscular dystrophy, myopathies and polymyositis.

b. Electric cardioversion.

c. Cardiac catheterization.

d. Hypothyroidism.

e. Stroke.

f. Skeletal muscles damage.

Secondary to trauma, convulsions and prolonged immobilization after cardiac surgery, myocarditis and electric cardioversion often result in elevation of serum levels of CPK MB - isoenzyme. The CK and LDH enzymes level generally do not rise in unstable angina.

CARDIAC IMAGING

Acute infarct scintigraphy (Hot spot) imaging is carried out with an infarct imaging agent such as (99_m Tc). Stannous pyrophosphate. Scans are usually positive 2-5 days after infarction particularly in patients of

transmural infarction. Myocardial perfusion imaging with thallium - 20/- or technetium 99 M Sesta-mibi which are distributed in proportion to myocardial blood flow and concentrated by viable myocardium reveals a defect (Cold spot) in most patients during the first few hours after development of transmural infarct. The wall motion abnormality determined by two dimensional echocardiography. It is also useful in diagnosis of right ventricular infarction, ventricular aneurysm, pericardial effusion and left ventricular thrombus, while Doppler echocardiography is useful in detection of VSD, MR and complication of acute myocardial infarction.

THROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION

1. Intracoronary Infusion

With catheterization intracoronary infusion of streptokinase is given within 3-4 hours of onset of symptoms have been shown to restore the patency of thrombosd artery in about 60 percent cases. In some patients immediate relief from angina isachieved and reversal of ST segment occurs and abnormal ECG towards normal ECG.

2. Intravenous Therapy

(A) Streptokinse

The streptokinase complexes with plasminogen which then converts circulating and fibrin fixed plasminogen to plasmin which lyses fibrin.

This streptokinase plasminogen complex results in circulation plasmin which causes systemic fibrinolyses with consumption of prothrombin factors V an VIII, Fibrinogen plasminogen and fibrin degradation products, it is antigenic.

(B). **Tissue plasminogen Activator rt PA**

Unlike streptokinase tpa is relatively thrombus specific there are two form of rtPA.

(A) - Alteplase (Single chain form)

(B) - Duteplase (Double chanin form)

(C). **Anistreptoplase or APSAC (An isolated plasminogen Streptokinase Activator Complex)**

This agent is a complex of streptokinase and lysoplasminogen with a P-anisoyl group placed in the catalytic centre of molecule in the intact stat. APSAC in an inactive complexbut when injected into the blood hydrolysis of anisoyl group occurs. Producing the active streptokinase plasminogen complexes, this produces fibrinolysis with a half of streptokinase that is 15-20 minutes and ultrashort half life of 5 minutes of tPA.

(D). **Urokinase**

(a). Urokinase acts on plasminogen coverting it to plasmin directly.

(b) Pro-urokinase : It is a single chain urokinase type plasminogen activator (SCU-PA) urokinase is not antigenic but it is not yet proved for use in acute myocaridial infarction.

The reduction in the mortality was inversely related to the time after onset of symptoms when streptokinase was given.

(i) Under I hour there was 50% reduction in the mortality rate.

(ii) Under 3 hours there was 25% reduction.

(iii) 3-6 hours 10% reduction in mortality rate and after 6 hours there was no any benefit GISSI trial (Grouppo Italiano, 1987) at 21 days rate was 1.7% in treated group and 13% in control group.

INDICATIONS FOR THROMBOLYTIC THERAPY

1. If ischemic symptoms persist more than 30 minutes that are associated with new ST segment elevation of at least 0.1 MV in at least two leads in the inferior, anterior or lateral location or ST segment depression in the anterior leads.

2. The thrombolytic therapy also indicated with different dose variations. These are :

   (i) Obstructive peripheral arteriopathies.

(peripharal arterial thromboembolisms).

(ii) Deep vein thrombosis and pulmonary embolism.

(iii) Ocular pathology -

3. a. Retinal vein thromboembolism.

b. Haemophthalmia.

c. Hyphaema.

CONTRAINDICATIONS OF THROMBOLYTIC THERAPY

A. **Abolute Contraindications**

1. Recent (within 2 weeks) invasive or surgicalprocedure or prolonged cardiopulmonary resuscitation.
2. Marked hypertension, if more than 180/100 mm Hg.
3. History of cerebrovascular haemorrhage.
4. Suspected Aortic dissection or pericarditis.
5. Haemorrhagic ophthalmic conditions such as diabetic haemorrhagic retinopathy.
6. Known allergy to streptokinase or APSAC (can be use tPA or urokinase).

B. **Relative Contraindications**

1. Head trauma or surgery of more than 2 weeks duration.
2. Recent severe hypertension with or without treatment.
3. Active peptic ulcer.
4. History of cerebrovascular accident.
5. History of bleeding diathesis or current use of anticoagulants.
6. Significant hepatic dysfunction.
7. Use of streptokinase or APSAC 6 months before

   (does not appoly to use of tPA or urokinase)

DOSES OF THROMBOLYTIC AGENTS

a. Urokinase : 2 millions IU I/V over 60 minutes.

b. Streptokinase ; 1.5 million IU I/V over 60 minutes. Heparin can be started I/V 4 hours after streptokinase and maintain for 48 hours.

c. Anistreplase (APSAC) : 30 mg I/V over 5 minutes (2-5 minutes).

d. tPA : 10 mg bolus I/V then 50 mg in 1st hour, 20 mg in 2nd and 3rd hours. Rapid or front leading - 15 mg bolus I/V 0.75 mg/kg over 30 minutes.

   50 mg over 60 minutes in both of these schedules the total does in 100 mg, heparin can be started I/V immediately after tPA and maintain for 48 hours.

e. tPA + SK : tPA 1 mg/kg over 60 minutes 10% as a bolus (total does 90 mg and SK 1 million units over 1 hour, start heparin after thrombolysis and maintain for 48 hours.

OVERALL COMPARISION OF VARIOUS THROMBOLYTIC AGENTS.

	STREPTOKINASE	UROKINASE	rt PA	APSAC
1. Usual doses	1.5 million units I/V in 30-60 mts.	2 million units I/V in 30-60mts	60 mg I/V in 1st hour na 40mg in 2nd-3rd hour	30 mg in 5 minutes..
2. Clot selectivity	None	None	Relative	minor
3. Patency of infarct related artery.	50-60%	60--75%	75-80%	-60%
4. Time depending	high <30%, after 4 hours	high <30% after 4 hrs	None	?
5. Reocculusion	5-20%	Similiar	10-20%	10-20%
6. Improvement of Lt ventricular Function	YES	YES	YES	YES
7. Improvement of Survival	YES	YES	YES	YES
8. Hypotension	Severe in <5%	Less Severe	NONE	NONE
9. Half life	long	long	short	long
10. Allergic Reaction	YES	No	No	YES
11. Fibrino genolysis	Severe	Severe	moderate	Severe
12. Intra cranial bleeding	<0.5%	<.5%	<.5%	<.5%
13. Repeat dosing Possible	No because of S.K. anti bodies	YES	YES	No
14. Cost	Less costly	Less costly then SK	More costly	Less costly then tPA

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The management of acute myocardial infarction has undergone a radical change during the last few years, with marked decrease in morbidity and mortality. The present mangement approach target of the complete or partial dissection or removal of thromobotic occlusion as a prime object to salvage jeopardised but salvageable tissue limit ultimately infarct size and preserve ventricular function as far as possible. This is based on available data indicationg that acute coronary thrombosis on a pre-existing atherosclerotic plaque is the usual cause leading to acute myocardial infarction. Several multicentric trials have demonstrated, the usefulness of thrombolysis in patients with evolving acute myocardial infarction. The benefits inculude (1) reuced early and late mortality (2) better maintained left ventricular function. It would thus appear rational to thrombolyse all patients with transmural acute myocardial infarction, but systemic thrombolytic state with fear of bleeding complications including death. This has led to development of criteria of exclusion and inclusion of partients for thrombolysis. Inspite of availability of a large body of data supporting its usefulness the number of patients who actually receive thrombolytic therapy is relatively small. Awasthi et al [8] have made an elegant attempt to define factors leading to non

administration of thrombolytic threapy to patients with acute myocardial infarction presenting to medical college hospitals in India.

Majority of patients did not receive thrombolytic therapy because of late presentation (beyond the time window of 6 hours) for various reasons or inability to reach a medical centre for other reasons. Even amongst those who reached the hospital within the specified time window more than 1/3 failed to receive treatment due to lack of awareness of the benefits of thrombolytic therapy, by physician, misreading of ECG, economic factor and refusal to consent for treatmet. Finally, only a small number of patients will be receiving thrombolytic therapy. The patients and primary physician related factors need mounting of a major education programme for the lay public and physicans regarding the clinical presentation of disease. There are enormous benefits of early thrombolytic therapy and thus the urgent need or the patients being referred to an emergency stantion or clinic at the earliest possible time after start of symptoms for receiving treatment. Economic factors including the high cost of the available in hospital emergency room and wards as such needs to be rectified. Such drugs should be categorised as life saving and given appropriate Government concessions and priorties for availavility in all hospitals. Several studies have show the feasibility and safety of thrombolytic therapy at home and in the coronary care ambulance

environments. Widening of time window beyond the conventional 6 hours for thrombolytic therapy especially in those with evidence of ongoing myocardial ischemia should be actively considered. It is usual to exclude patients over 70 years of age from the therapy because of reported higher incidence of intracranial haemorrhage. On the other hand large number of studies have shown that elderly patients receiving thrombolytic therapy had a lower mortality rate as compared to non thrombolysed patients.Althourgh the patients of anterior infarction benefit most from the treatment because of larger size of myocardium at risk, the benefits in the patients with infarior, posterior and lateral infarction are sufficient enough of justify the administration in evolving acute myocardial infarction It has resolutionized the management of such patients by reducing mortality by magnitude exceeding all previous treatment efforts. It is imperative that these benefits be available to largest possible of such patients. A large scale efforts in patient and physician education and a reconsideration and relaxation of criteria regarding patients selection for treatment is urgently required.

Almost all myocardial infractions result from Athrosclerosis of coronary arteris. generally with super imposed coronary thrombosis. A number of risk factors have been associated with development of atherosclerosis . The end result is plaque that causes minimal narrowing of coronary arterial tree and in many instances thrombus that causes further

narrowing and often total occulusion. Below a certain critical level of blood flow myocardial cells develop ischemic injury when severe ischemia is prolonged irreversible damage that is acute myocardial infarction occurs. Since the coronary lumiual narrowing affects the major coronary arteris and there various branches to a different extend acute myocardial infarction usually occurs focally in a specific region of heart. The location and size of the particular infarction depends on a number of different factors these are (1) Location and severity of the atherosclerotic narrowing in coronary arterial tree (2) Size of vascular bed perfused by narrowed vessel (3) The oxygen needs of poorly perfused myocardium (4) The extent of development of colloteral blood vessels (5) The presence, site and severity of coronary arterial spasm (6) The presence of tissue factors capable of modifying the necrotic process. 7. The activity and effect of endogenously released thrombotic and thrombolytic substances. The myocardial infarction may be divided into two major types A. Transmural Infarct :- In which myocardial necrosis involves the full thickness of ventricular wall B. SUBENDOCARDIAL INFARCTS or non Transmural infarcts :- In which the necrosis involves the subendocardium. The intramural myocardium or both without extending all the way through the venticular wall to the Epicardium. Acute coronary thrombosis appears to be far more common when infarction is transmural. The transmural infarction are more frequently localized to the zone of distribution of a single coronary artery. Non

transmural infarction however frequently appears in the setting of severely narrowed but still patent coronary arteris. In the presence of severe atherosclerotic narrowing of the coronary arteris with increased myocardial metabolic demands or decreased myocardial oxygen dilivery or both are capable of producing patchy non transmural myocardial necrosis. Which tends to involve the subendicardium myocardial infarction most commonly involves the Lt. ventricle and interventricular septum. however approximately one third to two thirds of patients with inferior infarction have some involvement of Rt. ventricle patients with pre existing Rt. ventricular hypertropy are predispose to develop Rt. ventricular infarction with acute inferior myocardial infarction. Isolated infarction of Rt. ventricle is seen in 3 to 5 percent of autopsy proven cases of myocardial infarction usually in patients of chronic lung diseases and Rt. ventricular hypertrophy.

At autopsy coronary arterial thrmobi which are appx. 1 cm in length in most cases adhere to luminal surface of an artery and are composed of platelets fibrin, enthrocytes and Leukocytes, the composition of thrombus or both distally varies at different levels. A white thrombus is composed of platelets, fibrin and a Red thrombus is composed of erythrocytes, fibrin, platelets and leukocytes proximally early thrombi are usually small and non acclusive and are composed almost exclusively of platelets.

Myocardial infarction generally occurs with abrupt decrease in coronary blood flow that follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis. The progression of the atherosclerotic lison to the point where thrombus formation occurs is a complex process related to vascular injury. The injury is produced or facilitated by factors such as cigarette smoking, hypertension and lipid occumulation. In majority of cases infarction occurs when a atherosclerotic plaque, fissures ruptures or ulcerates and with conditions favouring thrombogenesis(factors which may be local or systemic) mural thrombus forms leading coronary artery occlusion. Although in roughly in one half of cases no precipitating factors appears to be present prior to myocardial infarction triggers such as physical exercise, emotional stress. The onset of myocardial infarction may be at any time of day or night but a higher frequency occurs in morning within a few hours of awakening. Pain is the most common presenting complain in patients with myocardial infarction. The discomfort may be severe enough to describe as the worst pain the patient has ever experienced. The pain of myocardial infarction commonly used to describe it are heavy. squeezing and crushing. It is similar in character to the discomfort of angina pectoris but is usually more severe and last longer. Typically pain occurs in central portion of the chest, epigastrium and in about 30% cases it radiates to the arms (less common side of radiation includes the abdomen, back, lower jaw and neck). The pain of mycardial infarction may radiate as high as the occipital area. But

not below the unblicus. The pain is often accompained by weakness, sweating, nousea, vomiting, giddiness and anxiety. The discomfort usually commenses with the patient at rest when the pain begins during a period of exertion in contrast to angina pectoris it does not usually subside with cessation of activity. In about 15 to 20% patients myocardial infarction is painless. The incidence of painless infarction is greater in women and patients with diabetes mellitus and it increases with age. In elderly myocardial infarction may present as sudden onset of breathlessness which may progress to pulmonary oedema. The pain of myocardial infarction is similar to the pain of 1. Acute pericarditis 2. Pulmonary embolism 3. Acute aortic dissection 4. Costocondritis. Most patients are anxious and restless attempting to relief the pain by moving about in bed (squarming and streching about) pallor is common and often associated with perspiration and coolness of extremities. The combination of sub sternal chest pain persistant for more than 30 min. and diaphorisis strongly suggest acute myocardial infarction. In about 1/4 of the patients with anterior infarction have menifestions of sympathetic nervous system hyperactivity (Tachycardia and hypertension) and upto half of the patients with inferior infarction shows evidence of parasympathetic hyperactivity (Bradycardia, hypotension). Apical impulse may be difficult to palpate, other physical signs are in decreasing incidence S4 and S3 and transient apical systolic murmur, muscle disfunction (Pillary disfunction) during acute myocardial infarction. A pericardial rub is present in with transmural

myocardial infarction. Jugular venus distension occurs commonly in patients with right ventricular infarction. Temperature is elevated upto 38^0C during the first week following acute myocardial infarction and systolic pressure declines approx. 10 to 15 mmhg from the preinfarction state. In the diagnosis of myocardial infarction the earliest ECG changes is usually ST elivation later on there is diminution of size of R wave and in transmural infarction a Q wave begins to develop. Subsequently the T wave become inverted because of changes in ventricular repolarisation. This change persist after ST segment has returned to normal. The abnormalities are found in one or more leads from V1 - V4 in anteroseptal infarction while in anterolateral infarction produces changes from V4-V6, avl and in lead I, the inferior wall infarction is best seen in lead I and II avf the myocardial infarction causes a detectable rise in plasma concentration of enzymes which are normally concentrated within cardiac cells. The most important enzyme is creatine phosphokinese-MB (CPK-MB) which start to rise at 4 to 6 hours and peaks at about 12 hours and then falls to normal within 48 hours to 72 hours. The measurement of CPK-MB isoenzyme of myocardial is more specific for myocardial damage as CPK is also rises after intramuscular injection or after exercise because it also present in skeletal muscles. AST (aspartate amino transferase) start to rise about 12 hours after infarction and reaches to a peak in about second to third day and returning to normal with in 3 to 4 days. LDH starts to rise after 12 hours reaches a peak after 2 to 3 days and may remain elevated for a week or

more on blood examination leucocytosis is usually reaching a peak on the first day. ESR may remain raised several days. Chest radiograph may show pulmonary oedema which is not evident on clinical examination. Echocardiography detecting important complications such as cardiac rupture, VSD, MR and pericardial effusuion. In the management of myocardial infarction intravenus opiates (initially morphine sulphate 10 mg or diamorphine 5 mg) and antiemetic (initially cyclizine 50 mg or proclorparazine 12.5 mg) should be administered intravenusly through a canula, ASPIRIN administration of 150 to 300 mg per day improves survival (30% reduction in short term mortality) it inhances the the thrombolytic therapy. Thrombolytic therapy now a days most important step in the management of myocardial infarction is discussed in introductory part. Sublingual glyceryl trinitrate 400 to 500 micro grams is given in first aid measure. Intravenus NTG .6 to 1.2 micro gram per hour or isosorbite dinitrate are usefull in treatement of Lt. venticular failure, β blockers such as atenolol 5 to 10mg given over 5 min. intravenously or metoprolol 5 to 15 mg intravenus over 5 minutes. Releives pain reduces arrythmias and improves short term mortality. These drugs avoid in heart failure, heart block and in severe bradycardia, anti coagulants subcutaneous heparin 12,500 units twice daily for seven days or untill decharge from hospital. This reduces the risk of thromboembolic phenomenon.

AIMS OF STUDY

AIM OF STUDY

To find out whether thrombolytic therapy is of any use in decreasing infarct related short term complications and mortality as compared to non-thrombolytic conventional therapy.

MATERIAL AND METHOD

MATERIAL AND METHODS

The present study consisted of 40 patients, their age ranging from 38 years to 70 years with mean age of 51 years. These patients were admitted in intensive coronary care unit (ICCU) and emergency ward in M.L.B. Medical College hospital Jhansi (U.P.). These patients were divided into two groups.

1. **GROUP "A"** : - The group A consisted of 15 patients treated with thrombolytic agents. Out of 15 patients, two patients were females and 13 were males.
2. **GROUP "B"** : - The group B consisted of 25 patients treated with conventional methods. They did not receive thrombolytic therapy. Out of 25 patients, 2 were females and 23 patients were males. The standard criteria were used such as prolonged chest pain suggestive of acute myocardial infarction, arrival within 6 hours of symptom onset and an E.C.G. changes of ST segment elevation in two or more leads. Contraindications for thrombolytic therapy included such as Hypertension with Blood pressure > 180/110 mmHg, Diabetic Retinopathy, Bleeding diathesis, surgical treatment within 2 weeks and history of allergy to SK. Patients meeting these criteria were given intravenous STREPTOKINASE 7.5 lakhs to 1.5 Million units and average 1.4 million units or UROKINASE 7.5 Lakh units in 100 ml of 5% Dextrose water infused with in 60 minutes, along with ASPIRIN 150 mg once daily orally. Group B patients were given non-thrombolytic therapy because of the following reasons.

(i) Late arrival of patients in hospital beyond 6 hours of chest pain.

(ii) Cost of thrombolytic therapy which is most important. Many patients in India are unable to bear the cost of such drugs.

(iii) Lack of awareness of role of such thrombolytic drugs in patients and in general population.

(iv) Some Contraindications such as raised Blood pressure > 180/110 mm Hg.

(v) Misreading of ECG changes in aute myocardial infarction by physicians.

In both groups a complete history and examination done at the time of admmission. In group A the thrombolytic therapy was given between time interval of 2 hours and 5 $^{1}/_{2}$ hours. A thorough clinical examination and relevant investigation done like TLC, DLC, Hg%, Blood Urea, Blood sugar, Serum critinine, Serum cholestrol, Creatine Phosphokinase, (CPK), SGOT, SGPT, the electrocardiography has been recorded at the time of admmission to the hospital and complication during and after thrombolytic and non-thrombolytic therapy noted. The same procedure has been applied for the patients of Group "B". and after the treatment following comparision has been done between thrombolytic treated group and non-thrombolytic treated group.

i. Difference in the mortality between the patients of group A and group B.

ii. Effect on complications between two groups.

iii. Effect on ECG changes between two treated groups.

iv. Effect on serum enzymes between two treated groups.

OBSERVATION

OBSERVATIONS

The present study consisted of 40 patients their is age ranging from 38 years to 70 years with mean age of 51 years. These patients were admitted in intensive coronary care unit (ICCU) and in emergency wards of M.L.B. Medical College, Jhansi. Out of 40 patients 4 patients were females with an average age of 56 years. These patients were divided into group A and B on the basis of being treated with thrombolytic therapy and non-thrombolytic therapy respectively. Group A consisted of 15 patients and Group B 25 patients. In group A all the patients were treated with thrombolytic therapy. Out of total 15 patients in this group 14 patients recieved Streptokinase and only one patient received Urokinase. The Streptokinase was given in the dose of 7.5 lakh to 1.5 million units with an average dose of 1.4 million units, while Urokinase was given in the dose of 7.5 lakh units. The therapy was given between 2 to 51/2 hours of the onset of symptoms, with an average duration of 4 hours, while in group B none of the patients received thrombolytic therapy. The main factors responsible for not giving thrombolytic therapy were as follows.

1. Patient reaches in the hospital beyond the period of 6 hours.
2. Economic Factor - As all the patients had to purchase the very costly thrombolytic drugs themselves.
3. Severe hypertension (Blood pressure more than 180/110 mmHg) was responsible for not giving thrombolytic drug in 2 patients.

GROUP A

FOLLOWING PATIENTS ARE TREATED WITH THROMBOLYTIC THERAPY WITH THEIR GENERAL CHARACTERISTICS.

NAME OF PATIENT	AGE/SEX	RISK FACTORS	DIAGNOSIS	MORTALITY
1. MR. NIRBHAY SINGH	50/M	Hypertension Emo state	Acute antero-septal MI	-
2. PREMWATI	55/F	Hypertension obesity, Emo state	Inferior wall MI	-
3. MR. JAGDISH	40/M	Hypertension High fat diet	Acute antero-septal MI	-
4. MR. ASHOK KR. JAIN	45/M	Hypertension obesity, DM	Acute inferior wall MI	-
5. MR. JYOTI SWAROOP	50/M	Hypertension +ve F/H, Emo state	Acute inf wall MI	-
6. MR. AZAD VIR DUBEY	40/M	Smoking Alcohol,HT tabocco chewing	Acute inf wall MI	-
7. GOMTI	55/F	Obesity , Emo state High Fat diet	Acute antero-septal and posterior wall MI	-
8. MR. K.C. PALIWAL	50/M	Hypertension Emo state	Aucte antero-septal MI	-

NAME OF PATIENT	AGE/SEX	RISK FACTORS	DIAGNOSIS	MORTALITY
9. MR. R.B. SINGH	40/M	Tabacco chewing High Fat diet	acute inf wall MI with DM	NIL
10. MR. HARBANS SINGH	52/M	High Fat diet Emo stte	Acute Inf Wall MI with VT, cordiogenic shock	+ NT
11. MR. NAND KISHORE	72/M	Smoking,H.T. Tabacco chewing	Acute antero-lateral Lalitde wall MI	NIL
12. MR. K.D. SHARNA	45/M	Smoking, Hypertision Tabacco chewing	Acute antero-Lateral wall MI with RBBB	NIL
13. MR. HARBANS	60/M	Obesity,Hight Fat diet Emo state	Acute ant wall MI with CAD	" "
14. MR. KAMMOD	40/M	Smoking and tobacco chewing	Acute antero lateral wall MI	" "
15. SUNKE	55/M	Smoking,Tabacco chewing, emo state	Acute inf wall MI with COPD	" "

GROUP B

FOLLOWING PATIENTS ARE TREATED WITH NON-THROMBOLYTIC THERAPY WITH THEIR GENERAL CHARACTERISTICS

NAME OF PATIENT	AGE/SEX	RISK FACTORS	DIAGNOSIS	MORTOLITY
1. BHARI LAL	60/A	High Fat diet	ant. wall MI, with COPD with LVF with CAD with RBBB	Nil
2. Luxmi Parsad	70/M	Smoking High Fat diet,emo state	Acute antero-septal wall MI	" "
3. BABULAL JAIN	65/M	Hypertension +ve F/H, emo state	Acute antero-lateral wall MI	" "
4. BIHARILAL SONI	40/M	High Fat diet emo state	inferior wall MI with CAD	" "
5. VIDHYA DHAR	65/M	Smoking, Tobacco chewing, High Fat diet	Acute inf wall MI with CAD	" "
6. SADHU RAM	55/M	Smoking, Tobacco chewing, Alcohol	Ext ant. wall MI	" "
7. PALLU	40/M	Smoking Tobacco chewing, Alcohol	Acute inf wall MI	" "

NAME OF PATIENT	AGE/SEX	RISK FACTORS	DIAGNOSIS	MORTOLITY
8. ASHISH KR. MODI	38/M	Smoking Alcohol	inf well MI with Hypotension	+ nt
9. KALLY	42/M	Smoking Alcohol Tobacco Chewing	Acute inf wall MI with RBBB with IHD with Hypotension	" "
10. H.R. AGRAWAL	52/M	Smoking Alcohol Tobacco Chewing	Auite antero-lateral wall MI	Nil
11. Narain Das	42/M	Smoking, Alcohol Tobacco Chewing	Inf wall MI with CAD	" "
12. NIRPAT SINGH	45/M	Smoking, alcohol Tobacco Chewing	Acute antero lateral MI with hypotension	+ nt
13. HORI LAL	38/M	Smoking, alcohol Tobacco Chewing	inf wall MI	Nil
14. GOPLE	62/M	Smoking, alcohol Tobacco Chewing	Antero-septal wall MI with CAD	" "

NAME OF PATIENT	AGE/SEX	RISK FACTORS	DIAGNOSIS	MORTOLITY
15. MURARI SINGH	57/M	Smoking, alcohol Tobacco Chewing	Antero-lateral wall MI with CAD	+ nt
16. O. P. GOSWAMI	48/M	Hypertinsion Smoking alcohol, Emo state	inf wall MI	Nil
17. TULSA DEVI	55/F	Hypertension emo state	Acute antero-septal MI	" "
18. R.K. SEXENA	45/M	Smoking, alcohol	Antero-lateral wall MI with CAD	" "
19. R. S. Uppadhyay	52/M	Hypertision smoming	Acite inf wall MI with Hypotension	+ nt
20. Mahesh	65/M	Smoking , alcohol Tobacco Chewing	Acute antero septal MI with hypotension	" "
21. Munni Devi Shukla	58/F	Hypertinsion, emo state	Acute inf wall MI	Nil
22. R. Sharma	63/M	Hypertension Tobacco Chewing	Acute antero septal MI	" "

NAME OF PATIENT	AGE/SEX	RISK FACTORS	DIAGNOSIS	MORTOLITY
23. Kusheswar	65/M	Smoking, tobacco chewing	Acute inf wall MI with hypotension	+ nt
24. Ganga Prasad	46/M	Smoking,tobacco chewing	Acute anterior wall MI with hypotension	" "
25. Omprakash	40/M	Smoking, tobacco chewing	Inf. wall MI	Nil

SITE OF INFARCTION

In group A there were 9 patients of anterior wall myocardial infarction and 6 patients were of inferior wall myocardial infarction. Only one patient died in this group of inferior wall myocardial infarction, so that percentage of survival rate of thrombolytic therapy in anterior wall myocardial infarction is 60% and 33% in inferior wall myocardial infarction. While in group B 14 patients were of anterior wall myocardial infarction and 11 patients were of inferior wall myocardial infarction.

RISK FACTORS IN ACUTE MYOCARDIAL INFARCTION

In this study of all the 40 patients having exposure to various risk factors these are smoking, hypertension, diabetes mellitus, high fat diet, obesity and alcohol intake. The percentage of exposure to these risk factors were as follows :

Smoking	55%
Hypertension	37.5%
Diabetes mellitus	5%
High fat diet + obesity	25%
Alcohol intake	47.5%

Although alcohol intake always associated with some other risk factors such as smoking, hypertension etc.

CONVENTIONAL THERAPY

In both the groups following conventional therapy was given to the patients :

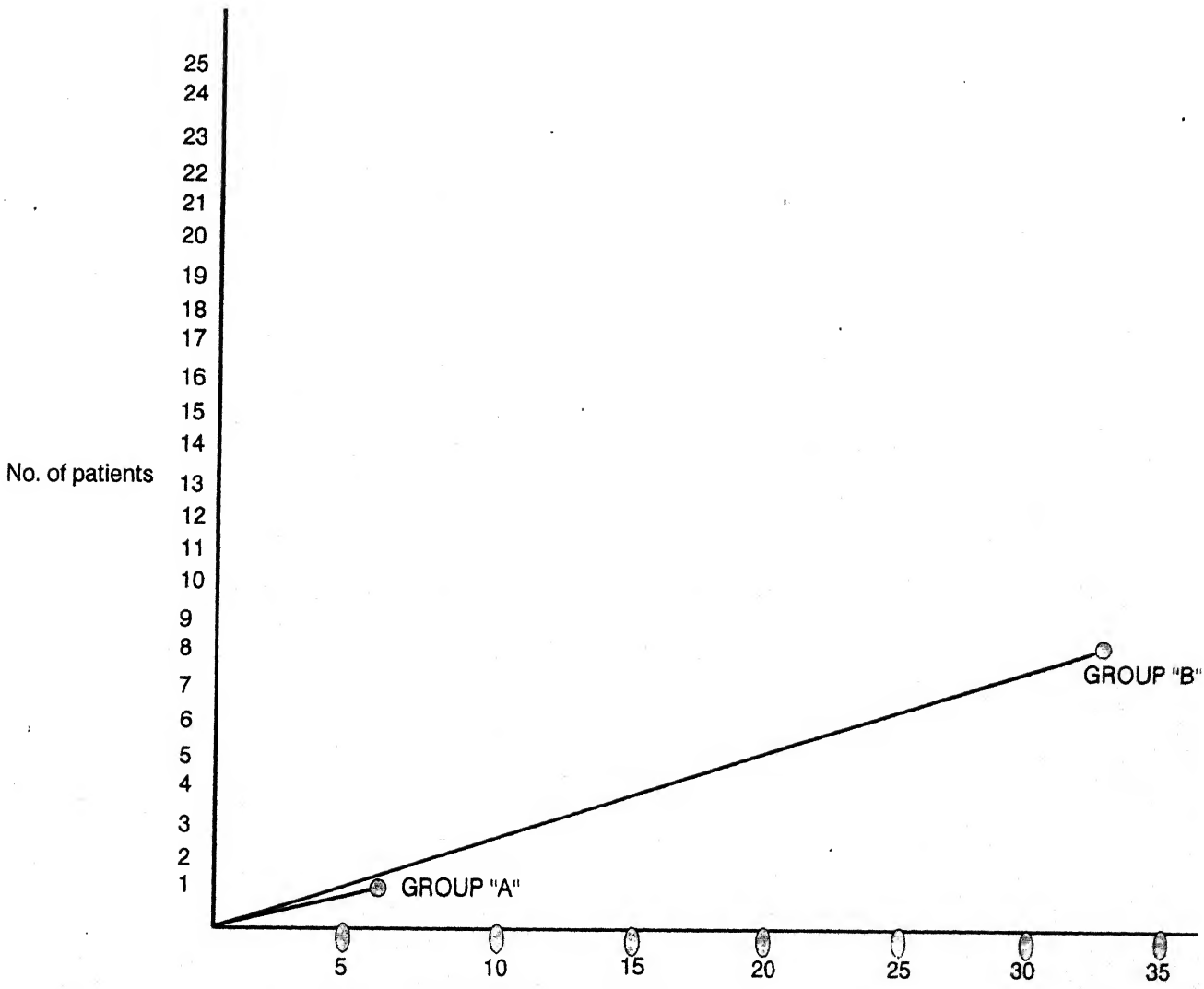
1. Injection Heparin 10000 units i/v stat and 5000 units i/v 6 hourly in 16 patients
2. Acetyl amino salicylic acid (Aspirin) is given to every patient in the dose of 150mg per day.
3. Sorbitrate - It was given to every patient in the dose of 10 mg 4 hourly and SOS, S/L.
4. Nitro glycerine - Injectible nitroglycerine given to 8 patients
5. Calcium channel blockers - Diltiagem was given in the dose of 30 to 60 mg thrice daily in 19 patients.
6. Angiotensine Converting Enzyme Inhibitor - Lisinopril was given in the dose of 2.5 mg to 5 mg daily in 13 patients.
7. β - blockers metoprolol in the dose of 50 mg twice daily in 19 patientsand Nefidipine 5 to 30 mg per day in 7 patients.
8. In all the hypertensive patients salt restriction was advised

ECG changes : The electrocardiographic changes in both groups

The ECG changes were studied at the time of admission in the hospital. In group A 8 patients had early settlement of hyperacute elevation of ST segment with in 6 to 8 hours while other 7 patients had ST segment settlement in 24 hours. The hyperacute elevation of ST segment in group B settledown between 24 to 72 hours, and only 4 patients having ST elevation beyond 4 days of acute myocardial infarction.

COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION IN BOTH GROUPS

S.No.	COMPLICATIONS	GROUP A		GROUP B		Reduction Of Complications in percentage
		NO Of Patients	Percentage	NO. Of Patients	Percentage	
i)	Multiple ventricular Ectopics	2	13%	10	40%	27%
ii)	Cardiogenic shock	2	13%	8	32%	19%
iii)	Recurrent Anginal pain (Post Acute MI)	3	19%	9	36%	17%
iv)	Atrial Fibrilation	1	6.6%	3	12%	5.4%
v)	Heart Block (2:1 A.V. Block or III degree A.V. Block)	0	0%	2	8%	8%
vi)	R.B.B.B.	1	6.6%	2	8%	1.4%
vii)	Left ventricular failure	0	0%	2	8%	8%
viii)	Atrial ectopics	2	13%	5	20%	7%



COMPARISION OF MORTALITY IN GROUP A AND GROUP B

SERUM ENZYMES

The serum enzymes investigated at the time of admission in this hospital are CPK-MB, SGOT, SGPT. The average rise of serum enzymes in group A were as follow ;

CPK-MB	83 U/L
SGOT	86 U/L
SGPT	85 U/L

while in group B average rise in serum enzymes were as follows :

CPK-MB	71 U/L
SGOT	87 U/L
SGPT	75 U/L

CAUSE OF DEATH - Ingroup A only one patient died due to cardiogenic shock and ventricular tachycardia

While in group B 8 patients died due to following complications:

i. Cardiogenic Shock
ii. Multiple ventricular ectopics
iii. Post myocardial infarction angina

Among 8 patients 6 died due to above mentioned complications while 2 died of left venticular failure, Atrial ectopic, R.B.B.B., post myocardial angina and complete heart block.

MORTALITY - The mortality in group A

Only 1 patient died in group A out of total 15 patients so there was only one mortality and the percentage of mortality in this group was 6.6% . The cause of mortality was cardiogenic shock with ventricular tachycardia.

While in group B there were 8 patients died out of 25 patients. These patients died due to complications of myocardial infarction such as cardiogenic shock, Recurrent anginal pain (Post MI), artial and ventricular ectopics, heart block, and R.B.B.B. so there was 32% mortality in group B and overall reduction in the mortality in thrombolytic treated group was 25.4%.

DISCUSSION

DISCUSSION

The present study included 40 patients, their age ranging from 38 years to 70 years with mean age of 51 years. These patients were admitted in intensive coronary care unit (ICCU) and emergency ward of M.L.B. Medical College, Jhansi. Out of 40 patients 4 patients were females with an average age of 56 years. These patients were divided into group A and group B on the basis of whether they were treated with thrombolytic therapy or not. The reason for not giving thrombolytic therapy were as follows :

1. Patients arrival in the hospital beyond 6 hours of onset of symptoms.

2. Economic factor - as all the patients had to purchase such costly drug themselves.

3. The severe hypertension - Blood pressure more than 180/110 mmhg was responsible for not giving thrombolytic therapy in two patients.

Comparative analysis of data from various thrombolytic trials

Study (year)	Total Patients	Inclusion criteria not met	Arrival after 6 hours	Inclusion criteria met	Contradictions
Murry et al. (3) (1987)	403	65%	39%	35 %	11%
Sainsour et al. (4) (1985)	1105	59%	44%	41%	8%
Present Study 1995	40	60.2%	60.2%	37.5%	5%
WilCox et al. Assett (9)(1990)	13282	46%	46%	54%	4%
Gissi -2(8) (1990)	38086	41%	41%	59%	11%

In group A all the patients were treated with thrombolytic therapy. Out of 15 patients in this group 14 patients received Streptokinase and only one patient received Urokinase. The Streptokinase was given with in average dose of 1.4 million units while Urokinase was given in the dose of 7.5 lakh units. Thrombolytic therapy was given between 2 hours to 51/2 hours of the onset of symptoms with an average duration of 4 hours. So percentage of patients received thrombolytic therapy with in 6 hours is 37.5% while 62.5% did not receive thrombolytic therapy.

In this study there were nine patients were of anterior wall myocardial infarction and 6 patients were of inferior wall myocardial

infarction. One patient died out of 6 patients with inferior wall myocardial infarction. So the study showed that thrombolytic therapy is more beneficial in anterior wall myocardial infarction as compared to inferior wall myocardial infarction. Various clinical trials - initial GISSI Trial [501] showed that thrombolytic therapy more successful in anterior wall MI rather than inferior wall MI. This trial shows that there is more successful rate in the anterior wall MI as compared to inferior wall MI. This trial also shows that benefit of thrombolytic therapy appears to be greatest when agents are administered as early as possible with benefit demonstrated if drug is administered less than 4 to 6 hours after the onset of chest pain and even better results are seen when drug is given less than 1 to 2 hours after symptoms start. The impact of early treatement was first clearly shown in initial GISSI Trial][501] and confermed in ISIS - 2 [502]. The relative benefit of thrombolytic therapy in inferior VS anterior myocardial infarction - initial results from the first GISSI Trial showed no improvement in survival for inferior wall myocardial infarction. More careful analysis of data has subsequently shown that infarct size rather than location is the key variable with no significiant benefit in the smallest of infarcts while the benefit (in terms of survival) increases with pergressively larger infarcts.

The present study and various trials had shown that thrombolytic therapy is more beneficial in anterior wall myocardial infarction as compared to inferior wall myocardial infarction.

In our study in group A only one patient died due to cardiogenic shock and ventricular techycardia. While in group B 8 patients died due to following complications

i. Cardiogenic Shock
ii. Multiple ventricular ectopics
iii. Post myocardial infarction angina

Among 8 patients 6 were died due to above complications and 2 patients were died due to Lt. ventricular failure, atrial ectopics , R.B.B.B., post myocardial angina and complete heart block. In the GISSI and ISIS-2[502] Trials a wide variety of other clinical benefits appears to patients treated with thrombolytic agents. Including reducing ventricular arrythmias i.e. asystole and cardiac arrest[502] as well as significiantly lower incidence of cardiogenic shock [544]. Longer term follow up is now available in early trials [545, 546], results indication that the early favourable results of thrombolytic therapy sustained over time with one study showing that the benefit of lower mortality is maintained over the 5 years follow up [546].

So the various trials of thrombolytic therapy as compared to our study is more or less similar.

In our study serum enzymes were investigated at the time of admission in this hospital. These are CPK-MB, SGOT, SGPT the average rise of serum enzymes in group A were as follows : CPK-MB 83 U/L, SGOT 86 U/L, SGPT 85 U/L. While in group B average rise in serum enzymes

were as follows : CPK-MB 71 U/L, SGOT 87 U/L, SGPT 75 U/L. So the average rise of these enzymes in both the groups having equal size of infarct.

AM Heart J - 1992 Apr study done at the university hospital Eppendorf, Hamberg, Germany. 84 cases with acute MI, total creatine Kinease, MB creatine kinease and MM Isoform determine at the start of thrombolytic therapy and 30 mins, 60 mins, 120 mins later the total creatine and MB creatine kinease increased significiantly at 60 mins. After start of thrombolysis and MMB creatine kinease activity and ratio MMB : MM1 had already increased at 30 mins. After the start of thrombolytic therapy the increased from base line of creatine kinease and creatine kinease MB activity were significiantly higher 120 mins after start of thrombolysis. Thus the rise in MMB creatine kinease in the ration of MMB : MM1 can be used for early detection of re-perfusion after intravenous thrombolytic therapy in acute myocardial infarction.

The electro cardiographic changes in both groups in the present study the ECG changes were studied at the time of admission in the hospital. In group A 8 patients having early settlement of hyperacute elivation of S.T. segment with in 6 to 8 hours. While other 7 patients having S.T. segment settlement with in 24 hours. The hyperacute elevation of S.T.

segment in group B settled down between 24 to 72 hours and only 4 patients having S.T. elevation beyond 4 days of acute myocardial infarction.

According to Z Kardio 1944 JUN ; 83(6) study done at Freie university at Berlin. 79 patients with acute myocardial infarction (pain < or = 6 hours). Continuous Holter monitoring of the infarct related S.T. elevation was initiated before or directly after starting thrombolytic therapy. During 24 hours observation period 34 patients (43%) showed episodes of recurrent S.T. elevation after an initial resolution (Group 1) among those with out episodes of S.T. elevation resolved within 4 hours in 34 patients (43%) group 2 and persisted > or = 4 hours in 11 (14% group 3). Episodes of reelevation were more frequently during the first four hours (.25 episodes per hour). Most episodes were transient and short lasting. Only 9 patients showed persistant re-elevation longer than 60 minutes. During hospitalisation in group 1 patients had a higher incidence of reinfarction and severe ischemic events than those without episodes group 1 12/34 (35%) Vs group 2 4/34 (12%) Vs group 3 1/11 (9%), P = .03).

In various trials and in our study showed that there is early return of S.T. segment elevation to the baseline after thrombolytic therapy.

In present study one patient died in group A out of 15 patients so there was only 1 mortality and percentage of mortality in this group was 6.6 percentage. The cause of mortality was cardiogenic shock and

ventricular tachycardia. While in group B 8 patients died out of 25 patients due to following complications like

i. Cardiogenic shock
ii. Recurrent anginal pain (Post MI)
iii. Atrial and ventricular ecotopics
iv. Heart block and R.B.B.B.

So there was 32% mortality in group B and overall reduction in mortality in thrombolytic treated group was 25.4%.

According GISSI [501] and ISIS [502] trials there is no doubt that early intravenous thrombolytic therapy improves survival in patients with acute myocardial infarction. A 30 days and 1 year mortality rate in some of the controlled trials are impressive with survival in 1 treated group as high as 93.1% at 12 months[541] mortality varies considerably depending on patients included for study and adjunctive therapy employed[528] . The benefit of thrombolytic therapy appears to be the greatest when agents are administered as early as possible. The benefit demonstrated when the drug is administered less than 4 to 6 hours after the onset of pain and even better results are seen when drug is given less than 1 to 2 hours after sympotms begins. ISIS -2 showed number of deaths among 563 patients. There is 8.0% death when the patients treated with Streptokinase along with aspirin and 10.4 % death when Streptokinase given without aspirin and there is 10.7 % deaths when only aspirin given.

According to int J Cardiol 1992 Nov 92 Department of medicine, Prince of Wales Hospital Chinese University of Honk-Kong.

102 patients received thrombolytic therapy the overall mortality is (18.6%) in the thrombolytic era, and for each sex and that for each sex 18.2% in males and 19.5% in females) were significiantly lower than those of pre thrombolytic era (27.1%, 23.4%, 37.7% respectively).

It has been shown from various trials as compared to our study that there is definite decrease in the percentage of mortality and complications after thrombolytic therapy.

SUMMARY & CONCLUSION

SUMMARY AND CONCLUSION

The present study included 40 patients. Their age ranging from 38 years to 70 years with the mean age of 51 years. These patients were admitted in intensive coronary care unit (ICCU) and emergency ward of M.L.B. Medical College, Jhansi (U.P.). Out of 40 patients four patients were females with an average age of 56 years. These patients were divided into two groups Group "A" and Group "B". On the basis of being treated with thrombolytic therapy and non-thrombolytic therapy respctively. The reason for not giving thrombolytic therapy in Group B were as follows :

i. Patients arrival in the hospital beyond 6 hours of onset of chest pain.

ii. Economic factor - as all the patients has to purchase such costly drug themselves.

iii. The sëvere hypertension - Blood pressure more than 180/110 mmhg was responsible for not giving thrombolytic therapy in two patients.

It has been shown that thrombolytic therapy is more beneficial in acute anterior wall myocardial infarction than acute inferior wall myocardial infarction. Because in group A 60% patients were of acute anterior wall MI and there was not a single mortality while 40% were of acute inferior wall MI and there was one mortality. So it has been shown

through this study that thrombolytic therapy is more beneficial in acute anterior wall MI as compared to inferior wall MI.

The effect of ECG changes after thrombolytic therapy in GroupA. 53 % patients showed early settlement of hyperacute elevation of S.T. segment with in 6 to 8 hours after thrombolytic therapy. While 47% ptients showed settlement of hyperacute elevation of S.T. segment within 24 hours. While in Group B 80% patients having S.T. segment settlement between 24 hours to 72 hours and only 20% patients having S.T. segment settlement after four days of admission in this hospital.

From the present study the is complications are also reduced to a much extent in group A as compared to group B. The percentage of reduction in the complications after acute myocardial infarction are as follows :

i) 27% reduction in the multiple ventricular ectopics
ii) 20% reduction in atrial ectopics
iii) 19% reduction in cardiogenic shock
iii) 17% reduction in recurrent anginal pain (post MI)
iv) 12% reduction in Atrial fibrilation.
vi) 8% reduction in heart block (2:1 AV Block or III degree heart block).

So it has been shown that thrombolytic therapy plays an important role in reduction of complications after acute myocardial infarction.

As far as mortality is concerned there is marked reduction in the mortality rate in thrombolytic treated group. There is overall 6.6 mortality in group A and 32% mortality in group B. Because of the reduction in the complications of acute MI there is 25.4% reduction in the mortality rate in thrombolytic treated group as compared to non-thrombolytic treated group.

Thrombolytic therapy is more beneficial in acute anterior wall MI and also in early settlement of hyperacute changes of ECG, more over thrombolytic therapy reduces mortality to a very much extent by reducing the complications of acute myocardial infarction.

WORKING PROFORMA

DEPARTMENT OF MEDICINE, M.L.B. MEDICAL COLLEGE, JHANSI

Dated :

NAME OF INVESTIGATOR : VIMAL KUMAR
NAME OF THE GUIDE : ASST PROF PRAVEEN KUMAR, MD (MED),DM (Card)
Place of Investigation : Hospital - M.L.B. Medical College, Jhansi
Ward/Bad -
Date of Examination :

A. **PERSONAL HISTORY**

1. Patient's name :
2. Age/Sex :
3. Religion :
4. Address :
5. Socio-economic status :
6. Sector : Rural/urban :

B. **RISK FACTORS**

i) **Major -**

1. Smoking
2. Tobacco chewing
3. Obesity
4. Alcoholism
5. Hypertension
6. Diabetes mellitus

ii) **Minor :**

1. Emotional state
2. Fat diet
3. Post MI and CAD

C. **CHIEF COMPLAINTS**

i)
ii)
iii)

D. **PRESENT ILLNESS**

E. **GENERAL EXAMINATION**

General condition			Cyanosis
Pulse rate			Jaundice
B.P.	:	Supine	Oedema
		Standing	hydration

Respiration
Temperature

CARDIOVASCULAR EXAMINATION

a. Inspection :
   i) Precordium
   ii) Apex beat
   iii) Other pulsations

b. Palpation :
   i) Apex beat
   ii) Thrill
   iii) Other pulsation

c. Purcussion :

d. Auscultation :
   i) Heart sounds :
      S1
      S2
      S3/S4

ii) Murmur : Systolic
Diastolic

RESPIRATORY SYSTEM

C.N.S.

ABDOMEN

LAB INVESTIGATIONS

TLC : Hb % :
DLC :
CPK - MB :
SGOT :
SGPT :
x-ray chest :
E.C.G. :
T. M.T. & Echo :
Echocardiography

TREATMENT

After how much time of chest pain thrombolytic therapy given :

Thrombolytic Therapy

	Name	Dose	Route of Administration	Duration
1.	Urokinase		Bolus/I.V. or	
2.	Streptokinase		in infusion	
3.	Any other			

Intravenous solution used ;
Inj. Hydrocortisone given or not :

Non-thrombolytic therapy

	Name	Dose	Duration	Rate	Route
1.	Heparin				
2.	Any other				

Additional drugs

1. Aspirin : Dose ;
2. Calcium channel blockers : Yes/No Dose :
3. Beta-blockers :
4. Nitrates : Dose : Route : Duration :

Investigation : CPK-MB

After how much hours of chest pain :

other Investigations, if done :

1.
2.
3.
4.

ANY COMPLICATION :

GENERAL EXAMINATION SUBSEQUENT DAYS

Day		Pulse	B.P.	R.R.	Temperature
1.	Morning				
	Evening				
2.	Morning				
	Evening				
3.	Morning				
	Evening				
4.	Morning				
	Evening				
5.	Morning				
	Evening				
6.	Morning				
	Evening				
7.	Morning				

Evening

OTHER EXAMINATIONS

1. J.V.P. :
2. Lungs ;
3. C.V.S. : S3/S4
4. Any arrhythmias :

CONCLUSION ON

Day 1st
2nd
3nd
4th
5th
6th
7th

Signature

REFERENCES

REFERENCES

1. De Wood MA, Spores J, Notske R et, Privalince of total coronary occulusion during the early hours of transmural myocardial infarction. N. Eng J Med. 1980 : 303 897-902
2. Kennedy JW, Ritche JL, Davis KB, et al. Western Washington randomized trial of intracoronary streptokinase in acute myocardial infarction. N Engl J Med 1983 ; 309 : 1477 1482
3. Gruppo Italiano per lo Studio della Streptochinasi nell' Infarto Miocardico (GISSI). Effectiveness of intravenous thombolytic therapy in acute myocardial infarction. Lancet 1986; 1:397-401
4. Gruppo Italiano per to Studio della Streptochinasi nell' Infarto Miocardico (GISSI). Long-term effects of intravenous thrombolysis in acute myocardial infarction : final report of the GISSI study. Lancet 1987 ; 2:871-874
5. ISIS-2 Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, or neither among 17,187 cases of suspected acute myocardial infarction. Lancet 1988 ; 2:349-360
6. Wilcox RG, Von der Lippe G, Olsson CG, Jenson G, Skene AM, hampton JR. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. Anglo-Scandinavian Study of Early Thrombolysis (ASSET) Lancet 1988; 2:525-530
7. AIMS Trial Study Group. Long-term effects of intravenous anistreplase in acute myocardial infaction : final report of the AIMS study. Lancet 1990; 335:427-431
8. Yusus S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction : overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. Eur Heart J 1985 ; 6:556-585
9. Muller DW, Topol EJ. Selection of patients with acute myocardial infarction fro thrombolytic therapy. Ann Intern Med 1990; 113:949-960

10. Topol EJ, Califf RM, Vandomael M, Grines CL, George BS, Sanz ML. et al and the Thrombolysis and Angioplasty in Myocardial infarction-6 Study Group. Arandomizedtrial of late reperfusion therapy for acute myocardial infarction. Circulation 1992;85:2090-2099

11. Late Study Group. Late Assessment of Thrombolytic Efficacy (LATE) study with alteplase 6-24 hours after onset of acute myocardial infarction. Lancet 1993; 342:759-766

12. EMERAS (Estudio Multicentrico Estreptoquinasa Republicas de American del Sur) Collaborative Group. Randomized trial of late thrombolysis in patients with suspected acute myocardial infarction Lancet 1993; 342 : 767-772

13. Fibrionlytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infaction : Collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet 1994 ; 343 : 311-322

14. Rentrop KP, Feit P, Sherman W, et al. Late thrombolytic therapy preserves left ventricular function in patients with collateralized total coronary occlusion : primary end point findings of the second Mount Sinai - New York University Reperfusion Trial. J Am Coll Cardiol 1989 ; 14:58-64

15. White MD, Norris RM, Brown MA, Brandt PWT, Whitlock RML, Wild CJ. Left coronary thrombolysis (recombinant tissuetype plasminogen activator) in preserving left ventricular function in acute myocadial infarction . AM J Cardiol 1990; 66 : 1281-1286.

16. Villari B, Pisicione F, Bonaduce D, Golino P, Ianzillo T, et al. Usefulness of late coronary thrombolysis (recombinant tissuetype plasminogen activator) in preserving left ventricular function in acute myocrdial infarction . Am J Cardiol 1990; 66 : 1281-1286.

17. Bonaduce D, Petretta M, Villari B, Breglio R, Conforti G, et al. Effects of late administraion of tissue-type plaminagen activator left ventricular remodelling and function after myocardial infarction. J Am Coll Cardiol 1990; 16: 1561-1568

18. Sager PT. Perlmutter RA., Rosenfeld LE, McPherson CA, et al. Electrophysiologic effects of thrombolytic therapy in patients with a transmural anterior myocardial infarction complicated by left ventricular aneurysum formation. J AM Coll Cardiol 1988 ; 12:19-24

19. Lange RA, Cigarroa RG, wells PJ, Kremers MS, Hillis LD. Influence of anterograde flow in the infarct artery on the incidence of late potentials after acute myocardial infarction. Am J Cardiol 1990 ; 65:554-558

20. Breithardt G., Borggrefe M, Karbenn U. late potentials as peredictors ofrisk after thrombolytic treatment ? Br Heart 1990 ; 64:174-176

21. Honan MB, Harrell FE, Reimer KA, et al. Cardiac rupture, mortality and the timing of thrombolytic therapy : a meta analysis . J Am Coll Cardiol 1990 ; 16:359-367

22. Dewood MA, Sores J, Notse RN, et al. Prevalence of total coronary artery occlusion during the early hours of transmural myocardial infarction, N Eng J Med 1981 ; 303 :897-902.

23. ISIS-3 a randomised comparison of streptakinase Vs tissue plasminogen activator vs antistreplase and of aspirin plus heparin vs aspirin alone among 41299 cases of suspected acute myocardial infarctiion Lancet 1992; 339 :753-67

24. Grines CL. Nissen SE, Booth DC, et al, A new thrombolytic regiment for acute myocardial infarction using combination half does tissue type plasmiongen activator with full dose streptakinase - A pilot study. J Am Coll cardiol. 1989;14 : 573-580.

25. Bode C, Schuler G, Nordt T, et al Intravenous thrombolytic therapy with a combination of single chain urokinase type plaseminogen activator in acute myocardial infarction. Circulation 1990;81:907-13.

26. Grines CL. Nissen SE, Boooth DC, et al. A prospective randomised trial comparing combination half does t-PA with streptokinase to full does preliminary report (abstr). J Am CollCardiol 1990; 15 : 4 A,

27. Proceedings of a symposium, thrombolytic therapy in cardiovascular diseases,- curent practices and future directions, Am J Med 1987 ; 83 (Suppl 2A) : 1-51.

28. Rimer KA, Lows JA, Rasmussen MM, Jennings RB. The wavefornt phenomenon of ischaemic cell death, Myocardial infarct size vs duration of coronary-occlusion in dogs. Circulation 1977 ; 56 : 786-94

29. Huey BL, Beller GA, Kaiser DL, Gibson RS. A comprehensive analysis of myocardial infarction due to left circumflex artery occlusion, comparison with infarction due to right coronary and left descending artery occlusion. J Am Coll Cardiol 1988 ; 12 :1156-66.

30. Wilcox RG, VonderLipper G, Olsson CG, Jenson G, Skene AM, Hampton JR, Trial of tissue plasminogen activator for mortality reduction-Anglo-Scandianavian study of early thrombolysis (ASSER). Lancet. 1988; 2:529-3-

31. Grouppo Italiano perlo studio delta streptochinsai nell Infarfomiocardio (GISSI). Effectiveness of Intravenous thrombolytic treatment in acute myocardial infaction. Lancet 1986 ; 1:397-402.

32. ISIS-2 (Second International study of infarct survival) collaborative group. Randomised trial of intravenousstreptokinase, oral aspirin both of neither among 17187 cases of suspected acute myocardial infarction : ISIS-2. Lancet 1988 ;2:349-50.

33. Yosuf S, Collins R, Petro R, et al. Intravenous and intracoronary Fibrinolytic therapy in acute myocardial infaction. Overview of results on mortality, reinfarction and sults on mortality, reinfarction and side effects from 33 randomized controlled triais. Eur heart J 1985; 6:556-85.

34. Topol EJ Armstrong PK, Vande Warf F, et al. Confronting the issues of patient safety and investigator conflict in interest of an international clinical trial in myocardial reperfusion. J Am Coll. cardiol 1992; 19:1123-8.

35. Nagel EL, Fine EG, Krischer JP, et al. Complications of cardiopulmonary resuscition. Crit Care Med 1981 ; 9:424.

36. Editorial, Reperfusion injury after thrombolytic therapy for acute myocardial infarction. Lancet 1989; 11:655-7,

37. Schoer DH, Ross AM. Wasserman AG,. Reinfarction, recurrent angina and reocclusion after thrombolytic therapy. Circulation 1987, 76:II-57-II-62.

38. Jalihal S, Morris GK. Antistreptokinase titres after intravenous streptokinase, Lancet 1990 ; 335:184-5.

39. TIMI study group : Comparison of invassive and conservative strategies after treatment with intravenous fissue plasminogen activator in acute myocardial infarction, Result of the thrombolysis in myocardial infarction (IIMI) Phase II trial. N Engl J Med 1989; 320 : 618-27.

40. Topol E, Califf R, George B, et al. A randomised trial of immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. N Engl J Med. 1987 ; 317 :581-88.

41. Simoons, ML, et al,. Thrombolysis with tissue plasminogen activator in acute myocardial infarction. No additional benefit from immediate percutaneous coronary angioplasty. lancet 1988; 1 : 197-202.

42. De Bono DR, Pocock SJ, the SWIFT study of intervention vesus conservative management after anistreplase thrombolysis, Br Med J 1991 ; 302 : 555-60.

43. De Wood MA. Spores J. Notske AR, Mouser LT. Burroughs R. Golden MS. Lang HT. Prevalence total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Medc 303 : 897, 1980.

44. Grouppo Italiano per lo studio delta streptochinasi nell infarmyocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1:397. 1986.

45. ISIS-2 (Second international study of infarct survival) Collaboration group (1988). andomized trial of intravenous streptokinase. or aspirin,both or nither among 17.187 cases of suspected acl myocardial infarction : ISIS-2. Lancet 2:346. 1988.

46. Sainsous J, Serradimjigmi A. Richard JL. Guizel. LeConte Taniellian PH. How many patients with acute myocardial infarction could be treated with intravenous streptokinse ? Results of a prospectivtrial (abstract). Eur Heat J 16 (Suppl II) : 67. 1985.

47. Murray N. Lyons J, Layton C, Balcon RO. What proportion of patient are sutiable for thrombolysis. Br Heart J 57 : 144. 1987.

48. Wilcox RG. VonDerlippe G. Olsson CG. Jensen G. Skene AM Jampton JR. Effects of alteplase in acute myocardial infarction:monts from the ASSET study. Lancet 335 : PII75,1990.

49. GISSI-2 : A factorial randomised trial of alteplase versus streptokinase and heparin versus no heparin among 12,490 patients with acute myocardial infarction. Gruppo

Italiano per lo studio Dell sopravviveza Nell infarto miocardico. Lancet 335 :65.1990.

50. Avasti G, Wander GS. Parti A and Anand IS. Feasibility of thrombolytic therapy-A one year prospective study Ind Heart J 44 :133, 1992.

51. Doulas W, Eisenberg MS. Martin JS. Litwin PE. Shacffer SM et al. Myocardial infarction triage and intervention project Phase I : Patent charcteristics and feasibility of prehospital initiation of thrombolytic therapy. J Am Coll Cardiol 15 : 986, 1990.

52. Roth A. Barbash GL, Hod H, Milter HI, Rath S et al. Should thrombolytic therapy be administered in the mobile intensive care unit in patients with evolving myocardial infarction? A pilot study. J Am Coll Cardiol 15 : 999,1990.

53. Second International Study of infarct survival (ISISII) Collaborative study group : Randomised trial of i.v. Streptokinase, oral aspirin, both of neither among 17, 187 cases of suspected acute myocardial infarction: ISIS 2, Lancet ii:349,1988.

54. GISSI, Long term effect of i.v. thrombolysis in AMI: Final report of the GISSI study . Lancet 2:871,1987.

55. Murray N, Lyons J, Layton C, Balcon R. What proportion of patients with myocardial infarction are suitable for thrombolysis. Br Heart J 57:144,,1987.

56. Sainsous J, Serradimigini A, Richard JL, Guize L. Le Conte T. Taniellian PH How many patients with acute myocardial infarction trial. (absetract)Eur Heart J.6 (Suppl 1) : 67,1985.

57. Burrell CJ, Skehan JD, Cowley ML, Barrett CW, Mills PG. Districts use of thrombolytic agents. Br Med J 300 :237, 1990.

58. Khaja F, Walton JA, Brymer JF et al. Intracoronary fibrinolytic therapy in Acute Myocardial infarction : report of a prospective randomi trial New Engl J Med 308:1305,1983.

59. European study group of steptokinase in acute myocardial infarction New Engl J Med 301 : 797,1979.

60. GISSI-2 : A factorial randomised trial of alteplase versus strepotokinase and heparin versus no heparin among 12490 patients with acl myocardial infarction.

Gruppo Italion Per-lo-Studio Del sopravvivza Nell Infarto Miocadico. Lancet 335 : 65, 1990.

61. Wilcox RG, Non Der lippe G, Olsson CG, Jensen G, Skene AM are Hamptton J. R. Effects of alteplase in acute myocardial infarction : months from the ASSET study. Lancet 335 : l175. 1990.

62. Lie Kl, Wallens HJ, Van Capelle FJ, Durrer D. Lidocaine in the prevention of primary ventricularfibrillation. A double blin randomised study of 121 consecutive patients. N Engl J Med 291: 132-1974.

63. Yusuf S, Sleight P, Rossi P, Ruduction in infarct size, arrhythmia and chest pain by early intravenous beta blockae in suspected acute myocardial infarction : Crirculation 67 (suppl): 32, 1983.

64. Rude RE, Poole WK, Muller JE, Turi Z, Rutherford J, et al. electrocardiographic and clinical criteria for recognition of acute 52:936,1983.

65. Zarling EJ, Sexton H. Milnor P Jr. Failur to diagnose acute myocardial infarction : the clinicopathological experience at a large community hospital JAMA 250 : 177, 1983.

66. Yusuf S, Pearson M, Steery H. The entry ECG in the early diagnosis and prognostic stratification of patients with suspected acute myocardial infarction. Eur Heart J. 5:716, 1984.

67. Wilcox, RG, Von der Lipps G, Olsson CG, Jensen G, Skene AM, Hampton JR : Trial of tissue plasiminogen activator for mortality reduction in acute myocardial infarction. Anglo scandinavian study of early thrombolysis (ASSET) Lancet 2:525, 1988.

68. Mathewson ZM, Mc Closkey BG., Evans AE, Russell CJ. Wilson C. Mobile coronary care and community mortality form myocardial infarction. Lancet i:441, 1985.

69. Bresnahan DR, Davis JL, Holmes J, Smith HC. Angiographic occurence and clinical correlates of intraluminal coronary artery thrombosis : role of ustable angina. J Am Coll Cardiol 6 : 285, 1995.

70. Gruppo Italiano Per Lo Studio Della Streptochinasi Nell Infarto Miocardio (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction Lancet ; 1: 397, 1986.

71. ISIS-2 (Second International Study of Infarct Survival) collaborative group. Randomised trial of intravenous steptokinase., oral aspirin, both or neither among 17, 189 cases of suspected acute myocardial infarction ISIS-2. Lancet : 2: 349, 1988.

72. Rentop P, Blanke H, Karsch KR et al. Selective intracoronary thrombolysis in acute myocardial infarction and unstable angina pectoris. Circulation 63:307,1981.

73. Vetrovec GW, Leinbach RC, Gold HK, Cowely MJ. Intracoronary thrombolysis in syndromes of ustable inschaemia ; angiographic and clinical results. Am Heart J. 104:946, 1982.

74. Mandelkorn JB.Wolf NM, Singh S et al. Intra-coronary thrombus in nontransluminal myocardial infarction and in unstable angina pectoris. Am J Cardiol 52: I, 1993.

75. Ambrose JA, Hjemdl-Monsen C, Borrico S et al. Quantitative and qualitalite effect of intacoronary strepokinase in unstable angina and non-Q infarction. J Am Coll Cardiol 9:1156, 1987.

76. Gotoh K, Minamino T, Katoh O et al. The role of intracoronary thrombus in unstable angina : angiographic assessment and thrombolytic therapy during ongoing angina attacks. Circulation 77 : 526, 1988.

77. De Zwaan C, Bar FW, Janssen JHA et al. Effects of thrombolytic therapy in ustable angina : clinical and angiographic results. J Am Coll Cardiol 12:301, 1988.

78. Harrison : Principles of Internal Medicine,
13th edition, 1994.

79. Hurst ; Text book of cardiology.

80. Brounwald ; Text book of cardiology.

81. Clinical cardiology by Cheitlin, Sockolow and Macilroy, 6th edition.

82. Principle and practice of medicine : Davidson, 16 th edition.

83. Clinical Medicine :Kumar and Clarks.

84. Indian Heart Journal : May - June, 1992.

85. Indian Heart Jounral: March/April, 1993.

86. Mediquest : Mediccal information servies by Ranbaxy, Vol 11, No. 3, 1993.

87. APT Text book of Medicine, 15 th edition.